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FULL PAPER

Potential of fermented kuini and ceri Terengganu beverages in enhancing insulin secretion in pancreatic cells

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Abstract

Kuini (*Mangifera odorata*) and ceri Terengganu (*Lepisanthes fruticosa*) are well-known indigenous fruit in Malaysia. Recently, the use of these fruits is gaining attention due to their high nutrient value. In this study, an antidiabetic activity was selected to be tested on the functional beverages from both fruits. A total of two products have been formulated based on the fermentation of kuini puree and ceri Terengganu juice. The study was conducted through an in vitro assay by using pancreatic cells (BRIN BD11). The pancreatic cells were incubated with KRB (negative control) or KRB-containing products (10-1000 µg/mL) or KRB containing glibenclamide (10-1000 µg/mL). Insulin concentration was determined using Rat INS (Insulin) ELISA Kit. Results showed that both fermented kuini and ceri Terengganu beverages have the ability to increase insulin secretion from BRIN BD11 cells as compared to the control. As for fermented ceri Terengganu beverage, the highest insulin secretion was observed at a concentration of 1000 µg/mL (3.51-fold of increment). Whereas for fermented kuini beverage, the highest insulin secretion was observed at a concentration of 500 µg/mL (3.38 -fold of increment). In conclusion, both fermented beverages have the potential to enhance insulin secretion from pancreatic cells. Further study is needed to be conducted through an in vivo experiment to verify the antidiabetic action of these fermented beverages.

1. Introduction

Diabetes mellitus is a metabolic disorder in the endocrine system. It is characterized by persistent high blood glucose levels (hyperglycemic state) resulting from a defect of insulin secretion and insulin action (Rahim *et al*., 2020). This chronic disease is reported in all parts of the world and becoming a serious threat to humans. Globally, it was reported that the number of people with diabetes was 154 million (in the year 2000) and expected to reach 154 million in the year 2025. Diabetes is also a major problem in Malaysia and is predicted to become a much bigger problem. The World Health Organisation (WHO) has estimated that in 2030, Malaysia would have a total number of 2.48 million diabetics compared to 0.94 million in 2000 – a 164% increase (Mafauzy, 2006).

Antidiabetic drugs such as metformin, glibenclamide, and tolbutamide are mostly practically used to control and treat diabetic patients (Wild *et al*., 2004). The anti-diabetic activity of these drugs would be categorized according to insulin sensitization, insulin secretion and extrapancreatic insulin release (Pandarekandy *et al.,* 2017). However, many scientists are still looking for alternative medicines from plants that have anti-diabetic properties. Plants such as fruits are the potential to be explored as antidiabetic food for humans.

Malaysia is one the countries which have a rich diversity of underutilized fruits that grow wild in the region of Peninsular Malaysia, Sabah and Sarawak. Some of these underutilized fruits are rarely eaten, unknown and unfamiliar. Based on the broad spectrum of their flesh and skin colour, these underutilized fruits may have potential benefits for human health (Hadijah *et al.,* 2020). In addition, some of these fruits have the potential to be used and processed as food products for local consumption. Based on ethnobotanical studies, many of the underutilised fruits and traditional vegetable species are the source of food and medicine for some communities in Malaysia. These species have great

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potential however, they are underexploited and not fully utilised. Research and development (R&D) in the Malaysian Agricultural Research and Development Institute (MARDI), especially on the bioprospection of underutilised fruits, indicated several potential species, such as ceri Terengganu, kuini dabai, kebayau, sentul and tengkawang (Mohd Shukri *et al*., 2013).

One of the underutilized fruits which is gaining attraction among researchers in Malaysia is ceri Terengganu or its scientific name *Lepisanthes fruticosa* (Roxb) Leenh. It is a non-seasonal underutilised fruit species that can be found in South East Asia which comprises Malaysia, Myanmar, Indo-China, Thailand, Philippines and Indonesia (Lim, 2013). The species is found growing naturally in forests and is mostly found growing as a home garden plant. Based on ethnobotanical studies, ceri Terengganu is usually consumed as a food source and is also used in traditional medicine by rural folks (Mirfat and Salma, 2015). It was reported that ceri Terengganu root has antipyretic properties and the ripe fruit has anti-diarrhoea properties (Wetwitayaklung *et al*., 2012). Ceri Terengganu has also been analyzed for its fibre content. Sabeetha *et al*. (2021) found that total dietary fibre in ceri Terengganu pulp and skin were 77.7% and 87.2%, respectively. The ceri Terengganu had the highest ash content which indicated that this fruit had the highest mineral content (Umi Kalsum and Mirfat, 2014). All samples also had high protein content which can be useful as food ingredients Besides, the safety assessment of ceri Terengganu has been conducted *in vitro* (Hadijah *et al*., 2020) and *in vivo* (Syahida *et al*., 2021). Based on these studies, ceri Terengganu was regarded as non-toxic and can be processed into functional food products.

Another rare fruit is kuini its scientific name is *Mangifera odorata*. It is a mango variety that belongs to the family Anacardiaceae. The fruit emits a fragrant smell, the flesh colour is light orange and juicy sweet when ripe (Salma *et al*., 2010). Kuini is native and can be found in South Asia, Malaysia, Indonesia, Thailand, Vietnam and the Philippines (Kiew, 2002). It was possibly represented a hybrid form between *Mangifera indica* and *Mangifera foetida* (Teo *et al*., 2002). Kuini fruits were used for making chutney and for pickles with salt. Previous studies showed that selected Mangifera species has high in antioxidants and nutrients including total phenolic as well as total flavonoid content (Mirfat *et al.,* 2016; Ismail *et al*., 2019). Khoo *et al.* (2008) also reported antioxidant activity from carotenoid content in *M. odorata*. Apart from that, recent studies discovered the prophylactic property of natural compounds in kuini seed extracts and could be used as an anti-Salmonellosis agent (Adnan *et al*., 2021). The effect of steaming and frozen storage on polyphenol content and antioxidant properties of kuini pulp had also been studied by Norra *et al*. (2021).

Fermented beverages hold a long history and have become an influential player in the global beverage economy, because of the growing demand for health products and their contribution to the nutrition of many societies worldwide (Liburdi *et al*., 2020). Fermented beverages have undergone a surge in popularity as a functional food choice, mainly due to their nutritional properties and proposed health benefits (Dimidi *et al*., 2019). Generally, nutritional attributes of food can be improved by fermentation, which may provide better organoleptic properties (such as taste, aroma, and texture) metabolism, digestion, absorption and favourable constituent of fermented food (Sanlier, 2017). Different yeast and bacteria (consortium) usually are mostly involved in the fermentation process, and as a result of their growth, more digestible and stable foods are produced (Salmeron, 2017). Studies have shown that the consumption of fermented foods and beverages may improve intestinal and extraintestinal health and might be useful in improving and treating infectious diarrhoea, reducing the duration and incidence of respiratory infections, and enhancing immune and anti-inflammatory responses (Kok and Hutkins, 2018; Sahu and Panda 2018). In addition, the fermentation process is one of the main options for processing foods in many developing countries, as it serves as an affordable and manageable technique for food preservation (Selhub *et al*., 2014).

Kuini and ceri Terengganu juices could serve as suitable media for cultivating a consortium of kombucha strains for fermented beverages production. The kuini and ceri Terengganu juices supplemented with sugar are allowed to ferment under aerobic conditions. The consortium of kombucha strains involves yeasts and acetic acid-producing bacteria that live together symbiotically to convert the sugared kuini and ceri Terengganu juices to form new fermented products through fermentation. The fermentation affected the physiochemical and sensory properties of the juices. With a focus on promising new value-added healthy products, the fermentation enhanced the antioxidant and antimicrobial activities of the resulting product, also were the bioactive compounds, with the desirable overall properties of the fermented beverages. A few studies carried out in MARDI revealed that the fermented kuini and ceri Terengganu beverages are a good source of bioactive compounds which make them as functional beverages (Adnan *et al*., 2019; Alyas *et al*., 2020; Musaalbakri *et al*., 2020a; Musaalbakri *et al.*, 2020b).

To date, the health benefit effect of fermented ceri

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Terengganu, as well as kuini beverages, are still lacking especially those focus on antidiabetic potential. Previous studies have shown that fermented products was able to exhibit anti-diabetic properties such as fermented jackfruit leaf beverages as compared to commercial anti-diabetic drugs with no adverse side effects (Koh *et al.,* 2020). Fermented fruit juice of *Morinda citrifolia* (mengkudu fruit) also potential to be the future nutraceutical beverage due to its antidiabetic and antioxidant activities (Simamora *et al*., 2019). In addition, plant medicine also become an alternative and popular in diabetic control as they are natural and considered to be less toxic and have side effects (Wang *et al*., 2016; Tafesse *et al*., 2017). The search for new, effective and safe therapeutic agents from natural resources has attracted much attention from many scientists around the world.

Therefore, the present study was performed to find possible antidiabetic activities of fermented ceri Terengganu and kuini beverages, if any, by evaluating the potential of these products to stimulate insulin secretion from pancreatic β cells. Glibenclamide, a commercial reference drug was also evaluated as comparison. The acute insulinotropic effects of these samples were performed on BRIN-BD11 pancreatic islet cells exposed to 2 mM glucose.

2. Materials and methods

2.1 Fermented kuini and ceri Terengganu beverages

The fermented kuini and ceri Terengganu beverages produced at the Malaysian Agricultural Research and Development Institute (MARDI) was used in this study. Kuini and ceri Terengganu juice supplemented with 15% (w/v) granulated sugar was prepared and pasteurised at 90°C for 10 mins. The juices were then inoculated with 10% culture containing the consortium of kombucha strains. The inoculated juices were fermented under static and aerobic conditions at 28°C for 21 days. Finally, the fermented kuini and ceri Terengganu juices were filtered using an ultra-filter (0.22 um) to obtain a final product free from microorganisms. The measured pH of the fermented kuini and ceri Terengganu was 2.50 and 3.25, respectively. The juices were kept frozen until further analysis. Liquid samples were freeze-dried prior to assay.

2.2 Cell culture preparation

BRIN BD11 cell line was a gift from the Animal Cell Culture Laboratory, Faculty of Biotechnology and Biomolecular Sciences, Universiti Putra Malaysia. 3T3F442A preadipocytes were purchased from the European Collection of Cell Cultures (ECACC, Salisbury, UK). ABRIN BD11 cells were maintained in a 75 cm^3 cell culture flask and cultured in RPMI- 1640 media supplemented with 10% FBS and antibiotics solution (50,000 IU/L penicillin-streptomycin) at 37°C humidified with 5% CO_2.

2.3 Insulin secretion assay

Insulin secretion assay was conducted according to the method of Adam *et al*. (2012) with brief modifications. Confluence BRIN-BD11 cells were seeded onto a sterile 12-wells plate at a concentration of $2.5x10^5$ cells per well and left overnight at 37°C to allow attachment prior to testing. The next day, cells were washed thrice with Kreb's-Ringer bicarbonate buffer (KRB) and pre-incubated with this KRB for 40 minutes at 37°C. Cells were further incubated for 1 hrs with 1 mL of KRB containing various concentrations of test samples (0-1000 mg/mL). All evaluations were performed at 2 mM glucose. Following incubation, 1 mL of aliquots from each well was transferred into 1.5 mL tubes and stored at -20°C for determination of insulin concentration. Glibenclamide was used as a positive control.

2.4 Determination of insulin concentration

Insulin release was determined using rat insulin ELISA kits (Elabscienceâ E-ELR2466 96T). 100 µL of samples and standard was added into the particular well of coated plate 96-well plate, covered with sealer and incubated for 90 mins at 37°C. The liquid was from each well and 100 µL was of Biotinylated Detection Ab working solution was added, the plates were covered, gently swirled and incubated for 1 hr at 37°C. After that, the liquid from each well were washed three times with 350 µL of washing buffer and dried. An aliquot of 100 µL of HRP conjugate working solution was added into each well, the plate was covered and incubated for 30 mins at 37°C. Again, the liquid was removed from each well, washed five times with 350 µL of washing buffer and dried. Substrate reagent was added at 90 µL into each well and incubated for 15 mins at 37°C (in a dark place). After that, the stop solution of 90 µL was added into each well. Lastly, the absorbance was read at 450 nm using EnspireâMultimode Plate Reader, (Perkin Elmer).

2.5. Statistical analysis

Results are expressed as mean ± standard deviation (SD) for a given number of observations (n = 6). Statistical analyses were performed using Student's T-test comparing treatments with a control. The group means were considered significantly different at the level of $p < 0.05$, 0.01 and 0.001.

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3. Results

3.1 Insulin secretion analysis of fermented ceri Terengganu beverage

The effects of fermented ceri Terengganu beverage (FCT) on insulin secretion from BRIN BD11 cells are shown in Figure 1. FCT exhibited a stepwise stimulatory effect on insulin secretion at 2 mM glucose. Significant stimulation was observed at concentrations 50, 100, 500, and 1000 µg/mL which evoked a 2.07-($p < 0.01$), 2.09 - ($p < 0.001$), 2.20 - ($p < 0.05$) and 3.51 -($p < 0.001$) fold of stimulation, respectively, compared to control (Table 1).

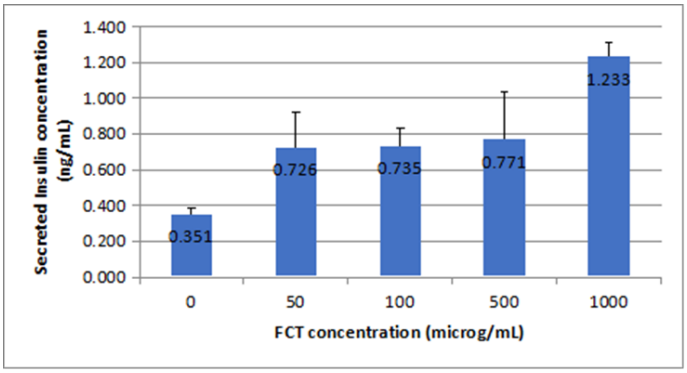

Figure 1. Insulinotropic effects of FCT on glucose-stimulated insulin secretion of BRIN-BD11 cells as compared with insulin levels under hyperglycaemic conditions (2 mM glucose). Values are presented as mean±SD (n = 6). The group means were considered significantly different at the levels *($p < 0.05$), **($p < 0.01$) and *** ($p < 0.001$) as compared with control.

This result showed that FCT has the ability to increase insulin secretion from BRIN BD11 cells compared to control (0 µg/mL). FCT exhibited a stepwise increment of insulin secretion up to a concentration of 1000 µg/mL. The highest insulin secretion was observed at a concentration of 1000 µg/mL (3.51-fold of increment).

3.2 Insulin secretion analysis of fermented Kuini beverage (FK)

Effects of fermented Kuini beverage (FK) on insulin secretion from BRIN BD11 cells are presented in Figure 2. Significant stimulation was observed at concentrations 50, 100, 500, and 1000 µg/mL which evoked a 2.69 - ($p < 0.01$), 2.37 - ($p < 0.05$), 3.38 - ($p < 0.01$) and 2.88 - ($p < 0.01$) fold of stimulation, respectively, compared to control (Table 2).

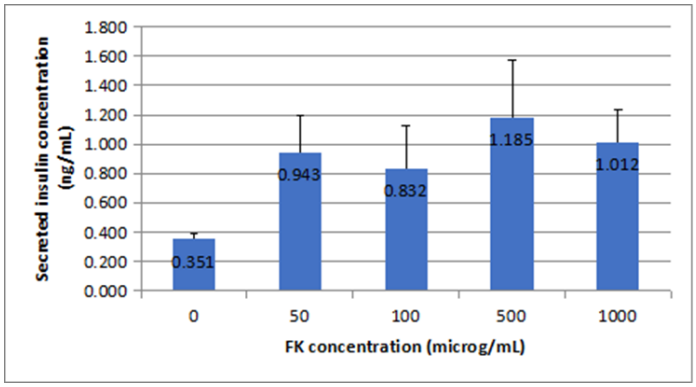

Figure 2. Insulinotropic effects of FK on glucose-stimulated insulin secretion of BRIN-BD11 cells as compared with insulin levels under hyperglycaemic conditions (2 mM glucose). Values are presented as mean±SD (n = 6). The group means were considered significantly different at the levels *($p < 0.05$), **($p < 0.01$) and *** ($p < 0.001$) as compared with control.

The result demonstrated that FK has the ability to increase insulin secretion from BRIN BD11 cells compared to the control (0 µg/mL). However, FK exhibited a fluctuating trend of insulin secretion. The highest insulin secretion was observed at a concentration of 500 µg/mL (3.38-fold of increment). The insulin secretion was noted to be reduced back at the highest concentration (1000 µg/mL) and achieved only 2.88-fold increment.

Table 1. Effect of FCT on insulin secretion (fold-increment).

	FCT concentration (µg/mL)				
	0	50	100	500	1000
R1	0.337	0.827	0.781	1.004	1.363
R2	0.356	1.038	0.784	1.026	1.229
R3	0.39	0.86	0.808	1.071	1.163
R4	0.357	0.456	0.546	0.549	1.175
R5	0.391	0.584	0.664	0.541	
R6	0.276	0.589	0.825	0.432	
Mean	0.351	0.726	0.735	0.771	1.233
SD	0.039	0.199	0.099	0.267	0.079
Fold-increment of insulin secretion compared to control (0)	1.00	2.07	2.09	2.20	3.51
Actual p-value (Paired Student T-test; two tailed distribution)		0.00786	0.00079	0.01406	0.00055
Significant level		p<0.01	p<0.001	p<0.05	p<0.001

All T-test were done against control (0 µg/mL). FCT: Fermented Ceri Terengganu.

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Table 2 Effect of FK on insulin secretion (fold-increment).

	FCT concentration (µg/mL)				
	0	50	100	500	1000
R1	0.337	1.109	1.405	1.335	0.978
R2	0.356	1.125	0.76	1.82	1.18
R3	0.39	1.124	0.532	1.171	0.69
R4	0.357	0.581	0.604	0.659	1.155
R5	0.391	1.115	0.698	0.764	0.764
R6	0.276	0.601	0.994	1.36	1.302
Mean	0.351	0.943	0.832	1.185	1.012
SD	0.039	0.249	0.294	0.390	0.223
Fold-increment of insulin secretion compared to control (0)	1.00	2.69	2.37	3.38	2.88
Actual p-value (Paired Student T-test; two tailed distribution)		0.00209	0.01962	0.00583	0.00219
Significant level		p<0.01	p<0.05	p<0.01	p<0.01

All T-test were done against control (0 µg/mL). FK: Fermented Kuini

3.3 Insulin secretion analysis of reference drug (glibenclamide)

The effects of glibenclamide on insulin secretion from BRIN BD11 cells are presented in Figure 3. Significant stimulation was observed at concentrations 50, 100, 500, and 1000 µg/mL which evoked a 2.43 - ($p < 0.01$), 2.57 - ($p < 0.05$), 6.77 - ($p < 0.001$) and 2.37 - ($p < 0.001$) fold of stimulation, respectively, compared to control (Table 3).

The result found that glibenclamide has the ability to increase insulin secretion from BRIN BD11 cells compared to the control (0 µg/mL). The highest insulin secretion was observed at a concentration of 500 µg/mL (6.77-fold of increment). This proved that the efficacy of glibenclamide in enhancing insulin was much better than the beverages. However, the insulin secretion was dropped back at the highest concentration significantly (1000 µg/mL) to be only a 2.37-fold of increment.

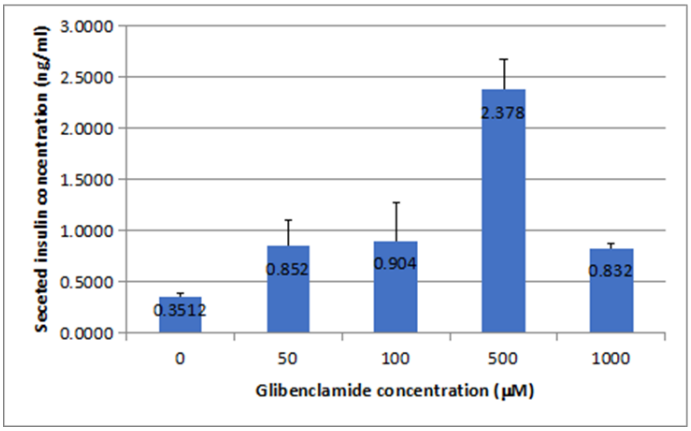

Figure 3. Insulinotropic effects of Glibenclamide on glucose-stimulated insulin secretion of BRIN-BD11 cells as compared with insulin levels under hyperglycemic conditions (2 mM glucose). Values are presented as mean±SD (n = 6). The group means were considered significantly different at the levels *($p < 0.05$), **($p < 0.01$) and *** ($p < 0.001$) as compared with control.

4. Discussion

Diabetes has been one of the top ten causes of

Table 3. Effect of Glibenclamide on insulin secretion (fold-increment).

	FCT concentration (µg/mL)					
	0	50	100	500	1000	
R1	0.337	1.12	0.459	2.599	0.78	0.78
R2	0.356	1.11	0.917	2.54	0.864	0.864
R3	0.39	0.705	1.138	1.94	0.758	0.758
R4	0.357	0.98	0.36	2.11	0.853	0.853
R5	0.391	0.772	1.349	2.26	0.892	0.892
R6	0.276	0.423	1.202	2.818	0.842	0.842
Mean	0.3512	0.852	0.904	2.378	0.832	0.832
SD	0.039	0.247	0.373	0.302	0.047	0.047
Fold-increment of insulin secretion compared to control (0)	1.00	2.43	2.57	6.77	2.37	2.37
Actual p-value (Paired Student T-test; two tailed distribution)		0.00509	0.02088	0.00004	0.00004	0.00001
Significant level		p<0.01	p<0.05	p<0.001	p<0.001	p<0.001

All T-test were done against control (0 µg/mL). Glibenclamide: Reference drug.

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death in Malaysia. A report from the Ministry of Health (MOH, Malaysia), revealed that 1 in 5 adults in Malaysia is having diabetes which is estimated about 3.9 million people (NHMS Report, 2019). The latest World Health Assessment for the year 2000-2016 showed that diabetes is one of the major diseases worldwide (WHO, 2016). A lack of effective insulin plays a key role in the development of diabetes. Insulin is a hormone that is responsible for allowing glucose in the blood to enter cells, providing them with the energy to function. Maintaining and promoting glucose-mediated insulin secretion is one of the major issues for diabetes therapy (Chang *et al.,* 2016). Therefore, an effective antidiabetic agent should both improve insulin sensitivity and enhance β cell function.

Nevertheless, both fermented ceri Terengganu and kuini beverages have never been investigated for their anti-diabetic effects through *in vitro* methods. Finally, it is described for the first time, the insulinotropic effect of fermented ceri Terengganu and kuini beverages which specifically focuses on their effects in stimulating insulin secretion from pancreatic β cell using BRIN BD11 cell line. Therefore, this study was conducted to evaluate the antidiabetic properties of these fermented beverages. This method was regarded as an acute evaluation to determine the potential of plants in enhancing insulin secretion (Opeolu, 2014; Faez *et al*., 2015; Yahaya *et al*., 2018). Stimulation of insulin secretion from pancreatic β cells is one of the mechanisms by which antidiabetic agents reduce hyperglycemia (Bosenberg and Van Zyl, 2008; Skelin *et al*., 2014). The secreted insulin will facilitate glucose uptake in insulin-sensitive cells such as muscle, liver, and adipocytes hence reducing hyperglycemia state (Adam *et al*., 2012). In addition. this method is also considered as a preliminary method for better screening before embarking on more costly tests such as animal testing using diabetic rats (Adam *et al*., 2012; Ansari *et al*., 2020).

In this study, insulin-secreting activity of fermented products (ceri Terengganu and kuini beverages) were evaluated in BRIN BD11 cells, a hybrid rat's pancreatic cell line. The results showed that all beverages significantly stimulate insulin secretion from BRIN BD11 cells at all concentrations evaluated (50-1000 µg/mL) with the magnitude of stimulations being from 2.07-fold to 3.51-fold compared to basal secretion. Among the two beverages, fermented ceri Terengganu exhibited the highest stimulation of insulin secretion at 1000 µg/mL (3.51-fold of increment) as shown in Table 1.

The optimum insulinotropic reaction of fermented kuini beverage can be achieved at 500 µg/mL (3.38-fold increment) as shown in Table 2. However, at the highest concentration, the insulin secretion slightly dropped, yet still higher than the control as presented in Figure 2. The cells could become saturated with the test substance, hence less insulin to be released. Adam *et al*. (2012) found the same pattern of low insulinotropic action in ethanolic as well as methanolic extract of *Ficus deltoidea* (Mas cotek) which might due to the presence of certain active compounds that damaged the pancreatic cells and less insulin was released.

From these findings, it is suggested that the optimum insulinotropic reaction of fermented ceri Terengganu beverage was at 1000 µg/mL. Whereas in fermented kuini beverage, its optimum concentration was at 500 µg/mL but still able to reach more than 3-fold increment.

As for comparison, the test also included glibenclamide, an antidiabetic drug. Glibenclamide is the most frequently prescribed as an oral hypoglycaemic agent (Nathan *et al*., 2009). It is a sulfonylurea compound that acts either as pancreatic or extra pancreatic, thereby increasing insulin release from the beta cells (Laxmi *et al*., 2009). The mode of action of glibenclamide in hyperglycaemic conditions is to lower blood glucose via stimulating insulin production from the existing beta cells of the pancreas (Rajasekaran *et al*., 2005). In this study, glibenclamide has demonstrated the most potent in insulin secretion at 500 µg/mL (6.77-fold of increment). On the other hand, the same pattern as in fermented kuini beverage was observed in glibenclamide. The concentration of insulin reduced at 1000 mg/mL indicating that this concentration could be toxic and disturb the cells from releasing more insulin (Figure 3). Our result is in agreement with a previous study by Laxmi *et al.* (2009), which suggested the insulinotropic effect of glibenclamide at a certain dosage only and the highest dose did not improve glycemic control and hyperglycemia continues to persist. In fact, it was found that increasing dose led to impairment of glycemic control rather than improvement.

Based on this present study, both fermented products may contain health-benefit compounds that exert their antidiabetic actions by stimulating insulin secretion from pancreatic β cells. There were a few studies reported earlier regarding the antidiabetic properties of ceri Terengganu. Mirfat *et al*. (2020) had focused on the evaluation of various crudes and fractions obtained from ceri Terengganu through α-glucosidase and α-amylase inhibitory activities. The results suggested that the ethanolic crude ceri Terengganu and its fraction could be an excellent source of bioactive phytochemicals with antidiabetic potential. The main explanation of the

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antidiabetic property of ceri Terengganu was mainly due to its antioxidant compounds as reported by Mirfat *et al*. (2017). The ripe fruits showed the highest free radical scavenging activity and had a great source of total phenolic contents among many other fruits tested. Phenolics are one of the major phytochemicals that contribute to the beneficial effects of plants for human consumption. Antioxidant-rich foods have significant antidiabetic potential and are widely used in the prevention and treatment of Diabetes Mellitus (Felipe *et al*., 2013; Arulselvan *et al*., 2014).

As for kuini, it is one of the mango (*Mangifera indica* L.) family, which is a good source of natural products such as polyphenols and phenolic acids, terpenoids and carotenoids (Lasano *et al*., 2019). The antidiabetic property may be due to similar compounds in Kuini too. Kuini also contains applicable amounts of antioxidants and total phenolic content (Mirfat *et al*., 2016). Evans *et al.* (2014) found that Mango juice supplementation managed to improve blood glucose levels in obese humans. Moreover, Samanta *et al*. (2019) also reported an antidiabetic activity of mango in different parts including seed and leave. A more recent study by Lasano *et al*. (2021) reported in vitro antidiabetic of the mangiferin-rich ethanolic extract of the pulp contributed to the α-amylase inhibition activity.

Fermented foods became an important part of the diet in many cultures, and over time fermentation has been associated with many health benefits. Lactic acid bacteria (LAB) have been some of the most studied microorganisms. During fermentation, these bacteria synthesize vitamins and minerals, produce biologically active peptides with enzymes such as proteinase and peptidase, and remove some non-nutrient (Sanlier *et al*., 2017). As a result, fermented foods provide many health benefits such as antioxidant, antimicrobial, antifungal, anti-inflammatory, antidiabetic and antiatherosclerotic activity (Sivamaruthi *et al*., 2018; Melini *et al.*, 2019).

However, some studies have shown no relationship between fermented foods and health benefits. Therefore, this paper aims to investigate the health effects of the newly developed fermented beverages. Recently, Musaalbakri *et al*. (2021) had reported the prebiotic properties in fermented ceri Terengganu beverage due to the Kombucha consortium used in preparing this product. On the other hand, nutritional, organic acid analysis, as well as antioxidant capacity, have been studied in fermented ceri Terengganu and kuini beverages (Musaalbakri *et al*., 2020a; Musaalbakri *et al*., 2020b). Both fermented beverages contained bioactive phenolic compounds such as gallic, syringic, caffeic, benzoic, ellagic ferulic acids and rutin (bioflavonoid). These compounds are suggested to contribute to their insulinotropic effects.

Kombucha products are well known for their health benefits and wellness humans (Watawana *et al*., 2015). At present, functional fermented beverages could be the most popular due to their convenience and possibility to meet consumer demands of handling container contents, size, shape, and appearance, as well as ease of distribution, storage, and opportunity to incorporate desirable nutrients and bioactive compounds (Corbo *et al*., 2014). A recent market study by Rawaida *et al.* (2020) revealed that both our fermented beverages were well accepted among Klang Valley consumers. Considering functional insulin receptors are known to be present in pancreatic beta cells and provide an important role in regulating glucose-mediated insulin secretion, insulinotropic effect of our fermented products might result from their insulin mimetic properties. On the other hand, the underlying mechanism to explain insulinotropic effect of both products remained to be investigated in future.

5. Conclusion

In conclusion, the present investigation provides novel evidence of fermented ceri Terengganu and kuini on insulin-secreting cells, BRIN-BD11 cells. The present study has revealed the presence of insulinotropic activity in fermented ceri Terenggani and kuini beverages. Both products indicated that they could ameliorate systemic insulin resistance and may potentially be beneficial for type 2 Diabetes Mellitus related to insulin resistance. Future works need to be conducted such as the antidiabetic activities through in vivo study by using antidiabetic rats for conclusive and more scientific evidence. Another important area is to profile the active compounds which contribute to the particular antidiabetic actions and their mechanism. Continue research may provide new opportunities for the treatment of diabetes that are safe, efficient and exert a lesser amount of side effects.

Conflict of interest

The authors declare no conflict of interest.

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